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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,215	06/24/2003	Neema M. Kulkarni	PC 21501B	2258

28880 7590 12/01/2006

WARNER-LAMBERT COMPANY
2800 PLYMOUTH RD
ANN ARBOR, MI 48105

EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,215	KULKARNI ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18 and 19* is/are pending in the application.

4a) Of the above claim(s) *19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 9/21/2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Election/Restrictions

Newly submitted claim 19 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the newly submitted claim is a method of treatment claim whereas the originally claimed invention was drawn to compositions.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 19 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR § 1.142(b) and MPEP § 821.03.

Status of the Claims

Claims 1-14 and 18-19 are currently pending and are the subject of this Office Action. Claim 19 is withdrawn from further consideration. Claims 1-14 and 18 are presently under examination.

Response to Arguments

Applicant's arguments filed 9/21/2006 have been fully considered but they are not persuasive. Applicants argue, *inter alia*, that the combination of the WO '573 and Zour *et al.* references do not render the instant claims obvious because "modifying the '573 reference as suggested by the Office action would change the principal operation of the reference." Applicants further argue that applicant's invention has discovered that gabapentin or pregabalin can be formulated in stable liquid pharmaceutical compositions having low levels of lactam when the pH of the composition is about 5.5 to about 7 and when the composition includes one or more polyhydric alcohols (*e.g.* xylitol). Applicants allege that the compositions of '573 require the presence of an additional amino acid to inhibit lactam formation, and therefore its absence would "change the principal operation of the reference."

Applicant's arguments have been considered but are not persuasive. WO '573 discloses compositions comprising gabapentin (5 g/100 mL), xylitol (15 g/100 mL), and water (page 44, Example 2(e) and page 45, Table 4).[1] Although lactam formation does increase in the presence of xylitol (Table 4), the increase is no different than that observed in applicant's own experiments (see Cai Declaration submitted 4/7/2006).[2] For example, in the presence of xylitol (15 g/100 mL) from a pH of 5.0 to 6.0, gabapentin lactam formation increases, just as in the composition disclosed in WO '573. Thus, it is not clear to the examiner how the composition disclosed in WO '573 is different from the claimed composition. It is only from pH 6.5 to 7.3

[1] Examiner has not made a 35 U.S.C. 102 rejection (anticipation) because the WO '573 reference does not disclose the pH of the solutions.
[2] It is noted that the instant claims do not recite that the claimed compositions will result in decreased lactam formation.

that lactam formation decreases in the presence of xylitol (Table 2, Cai Declaration). However, as noted in the previous Office Action, there is clear motivation to formulate a gabapentin composition at a pH from about 5.5 to 7 because Zour *et al.* disclose that liquid formulations of gabapentin are stable (*i.e.* less lactam formation) in this pH range (see especially Fig. 6, page 598).

Thus, examiner maintains that a composition of gabapentin, xylitol, and water (disclosed in WO '573) formulated at a pH from 5.5 to 7.0 (disclosed in Zour *et al.*) would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Examiner reminds applicants that WO '573 anticipates a composition comprising gabapentin, xylitol, and water because the reference explicitly formulates and tests such a composition. Zour *et al.* is only required in the instant 35 U.S.C. § 103 rejection because WO '573 does not disclose at what pH the composition was formulated.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-14 and 18 are again rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 99/59573 in view of Zour *et al.* (Pharmaceutical Research, 1992, v. 9, pp. 595-600).

The '573 reference discloses solid and liquid pharmaceutical compositions comprising gabapentin analogs with increased stability (Abstract). The compositions further comprise amino acids that are disclosed as agents capable of inhibiting lactam formation (page 10, lines 1-12). Sweetening agents, such as mannitol and xylitol may also be added to the compositions "if needed" (page 41, lines 21-22).

Zour *et al.* disclose stability studies of gabapentin in aqueous solutions (Abstract). The reference demonstrates that the stability of gabapentin in aqueous solution is greatest at a pH of 6.0, and at 45 °C gabapentin demonstrated minimal degradation when formulated at a pH from 5.5 to 7.0 (see especially Fig. 6, page 598).

Thus, it would have been *prima facie* obvious to modify the compositions disclosed in the '573 patent by formulating them at a pH of 5.5 to 7.0 as disclosed in Zour *et al.* The skilled artisan would be motivated to do so because Zour *et al.* disclose that formulations of gabapentin in aqueous solutions show minimal degradation when formulated at these pHs. The skilled artisan would have been imbued with at least a reasonable expectation that a solution of gabapentin and xylitol would exhibit less lactam formation (*i.e.* would be stable) at a pH of 5.5. to 7.0.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

November 15, 2006

PHYLLIS SPIVACK
PRIMARY EXAMINER
11/16/06